REMARKS/ARGUMENTS

Status of Claims and Specification

After entry of this amendment claims 1, 4-14, 17-22 and 25-27 are pending. Claims 2-3, 15-16, and 23-24 have been canceled. Independent claims 1, 14, 19 and 20 have been amended to recite that the introduced nucleotide sequence encodes an enzyme that catalyzes the synthesis of cytokinin. Support for these amendments is found, for example, in the canceled claims. Claim 7 has been amended to delete reference to 70% identity. Claims 4, 17, and 25 have been amended to delete reference to canceled claims. No new matter is added with these amendments.

Claims 1-27 stand rejected under 35 U.S.C. § 112, first paragraph, for allegedly lacking written description and enablement. The same claims stand rejected under 35 U.S.C. § 103(a) for allegedly being obvious over Amasino *et al.*(US Patent No. 5,689,042). Each of these rejections will be addressed below.

In the Office Action, the specification was objected to for relying on Gan *et al. Science* 270:1986-1988 (1995) for disclosure of the isopentenyl transferase (IPT) enzyme. In fact, in paragraph 71 of the specification, applicants cite a number of references for the sequence of this enzyme. One of the citations is GenBank Accesson NC_03308, which has been incorporated by reference (*see* paragraph 73 of the specification). A copy of the GenBank Accession is attached as Exhibit 1 to this amendment.[1] In addition, the Sequence Listing has been amended to include this sequence. Applicants believe that in light of the above, the specification provides full disclosure of the IPT enzyme.

This amendment is accompanied by a floppy disk containing all sequences disclosed in the application in computer readable form, and a paper copy of the sequence information which has been printed from the floppy disk. The information contained in the computer readable disk was prepared through the use of the software program "PatentIn" and is identical to that of the paper copy. This amendment contains no new matter.

The Present Invention

The present invention is based, at least in part, on the discovery that inhibiting programmed cell death in the lower floret of a maize plant provides plants having kernels with multiple embryos. Because most of the oil and protein in maize kernels is present in the embryo, maize plants with multiple embryonic kernels contain more protein and oil than maize plants having kernels with one embryo. Thus, based on this discovery those of skill can now produce maize plants having kernels with increased nutritional value. As explained below, the invention is thus not the discovery of particular genes or promoters that can be used to inhibit programmed cell death in the lower floret, but the discovery that preventing death of the lower floret is useful in producing maize kernels of increased value.

Rejections under 35 U.S.C. § 112, first paragraph

Written Description

The written description rejection is based on an allegation that the specification fails to provide adequate description for either the gene used to inhibit programmed cell death or the promoter used to target expression to the appropriate tissue. As noted by the Examiner, the specification specifically discloses the use of the SAG12 promoter to drive expression of the IPT gene in cells undergoing programmed cell death.

This rejection appears to be based primarily on an assertion that promoters at least 70% identical to the exemplified SAG12 promoter lack written description. To expedite prosecution, claim 7 has been amended to be directed to the SAG12 promoter as set forth in SEQ ID NO: 1. Applicants specifically reserve the right to pursue the original scope of claim 7 in one or more subsequent applications. The remainder of the rejection appears to be largely based on a concern that the promoters and genes used in the methods of the invention are defined primarily

[1] GenBank Accession consists of 129 pages and is the complete sequence of the *Agrobacterium* Ti plasmid. Exhibit 1 provides only the first 69 pages, which disclose all of the open reading frames in the sequence. The IPT protein sequence is disclosed on page 6.

by their function. As explained below, description of nucleic acids by function is not necessarily a basis for a rejection for lack of written description.

The written description requirement is satisfied when the specification describes the claimed invention in sufficient detail that one of skill in the art can reasonably conclude that the inventor had possession of the claimed invention (*see, e.g.*, MPEP § 2163(I), citing *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 19 USPQ2d 1111 (Fed. Cir. 1991).

According to the Federal Circuit, Applicants have some flexibility in the "mode selected for compliance" with the written description requirement. *University of Rochester v. G.D. Searle & Co.*, 69 USPQ2d 1886, 1896 (Fed. Cir. 2004). Moreover, it is well settled that the description need only describe in detail that which is new or not conventional. *See Hybritech v. Monoclonal Antibodies,* 231 USPQ 81, 94 (Fed. Cir. 1986); M.P.E.P. 2163.

There is, however, no ban on functional language to define nucleic acids. The Federal Circuit has stated: "It is not correct . . . that all functional descriptions of genetic material fail to meet the written description requirement." See *Enzo Biochem Inc. v. Gen-Probe Inc.*, 296 F.3d 1316, 1324, 63USPQ2d 1609, 1613 (Fed. Cir. 2002). See also *Moba B.V. v. Diamond Automation Inc.*, 325 F.3d 1306, 1320, 66 USPQ2d 1429, 1439 (CA FC 2003) (stating "[m]ore recently, in *Enzo Biochem*, we clarified that *Eli Lilly* did not hold that all functional descriptions of genetic material necessarily fail as a matter of law to meet the written description requirement; rather, ***the requirement may be satisfied if in the knowledge of the art the disclosed function is sufficiently correlated to a particular, known structure***. *Amgen*, 314 F.3d at 1332") (emphasis added).

As noted above, the pending claims are directed to inhibiting programmed cell death in the lower floret of a maize plant by specifically expressing an enzyme involved in cytokinin synthesis in the cells of the lower floret. The promoter can be one that is induced in response to programmed cell death or one that directs expression in the lower floret. As acknowledged by the Examiner, the SAG12 promoter is an exemplary programmed cell death specific promoter. As also noted by the Examiner, the prior art has used the SAG12 promoter to direct expression in senescent tissue. Moreover, the prior art provides structural information about the SAG12 promoter that correlates with its particular function. In fact, prior art studies

using promoter deletions and recombination of promoter fragments indicate that a highly conserved region of the SAG12 promoter is responsible for senescence-specific regulation, while at least two other regions of the SAG12 promoter are important for full promoter activity (*see* Noh *et al. Plant Mol Biol.* 41:181-94 (1999), Exhibit 2. Thus, applicants provide an exemplary promoter for which the disclosed function is correlated to a particular, known structure.

With regard to promoters that direct expression to the lower floret, the specification provides numerous examples of genes whose expression is lower floret-specific (*see* Specification paragraph 56). Indeed, one gene *Tasselseed2* is induced by programmed cell death in the lower floret.

Similarly, the protein expressed in the invention is one that is involved in cyotinin synthesis. An exemplary enzyme, IPT, is disclosed. Again the disclosed function is sufficiently correlated to a particular, known structure. As noted in the Li *et al.* reference cited by the Examiner, genes encoding this enzyme have been introduced into plants as early as 1989 (*see* Li *et al.* page 386, first column). Examiner has identified nothing to show that one of skill would not appreciate that its function is correlated to a particular, known structure.

In light of the above , applicants respectfully submit that the Examiner has failed to establish that the written description is not met. As noted above, applicants have flexibility in complying with the written description requirement. In the present invention, the invention lies in the discovery of the beneficial effects of inhibiting programmed cell death in the lower floret of maize plants, not the particular nucleic acids used to achieve this effect. Thus, one of skill reading the present disclosure would appreciate that the inventors were in the possession of the present invention. In addition, to the extent the rejection relies simply on an assertion that a functional description of nucleic acids is improper, the rejection cannot be maintained. The written description requirement may be satisfied if in the knowledge of the art the disclosed function is sufficiently correlated to a particular, known structure. As shown above, the structure and function of promoters and genes useful in the invention were known in the art. Withdrawal of the rejection is respectfully requested.

Enablement

The claims also stand rejected for lacking enablement because it would allegedly require undue experimentation to practice the claimed invention. The Examiner acknowledges that the specification enables the use of the SAG12 promoter linked to the IPT gene, but alleges that undue experimentation would be required to make and use other embodiments within the scope of the claims.

The Court of Appeals for the Federal Circuit has long recognized that in a rejection for undue experimentation that: "the key word is 'undue', not 'experimentation'". *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988). This decision makes clear that a considerable amount of experimentation is permissible if it is merely routine, or if the specification provides a reasonable amount of guidance respect to the direction in which the experimentation should proceed. The MPEP reiterates this same conclusion (*see*, MPEP § 2164.06).

In an attempt to support the assertion that undue experimentation would be required, the Examiner states that applicants have not disclosed how one isolates other programmed cell death inducible or floret-specific promoters. In fact, the specification provides a thorough discussion of how to identify promoters useful in the invention. Pages 11 to 13 of the specification describe means for identifying cells undergoing programmed cell death, means for identifying mRNAs that increase in abundance during programmed cell death, means for isolating cDNAs corresponding to the mRNAs, and means for finding promoters in genomic DNA that corresponds to the cDNAs. Means for testing whether a promoter is, in fact, induced in response to programmed cell death are also disclosed.

In addition, at paragraph 55, applicants discuss how the SAG12 promoter can be used to identify related promoters in *Arabidopsis* or other plants. Indeed, two maize genes with significant similarity to the SAG12 gene are identified. Moreover, as discussed above, Noh *et al.* (Exhibit 2) used standard deletion analysis to identify regions in the SAG12 promoter that confer the desired expression pattern. This publication shows that after a particular promoter of interest is identified, engineering new promoters with desired expression is well within the skill in the art.

In paragraph 56 of the application, applicants provide a number of floret-specific genes whose promoters can used to specifically express desired nucleic acids in these tissues. It is also clear that orthologs of these genes can be identified in other species using well known techniques.

The Examiner also alleges that applicants do not provide information about genes useful in the present invention. Again, the Examiner's attention is drawn to pages 14 to 17 of the present specification. There, applicants discuss plant growth regulators that are known to promote programmed cell death (*e.g.*, ethylene and gibberelic acid) and plant growth regulators that are known to inhibit programmed cell death (*e.g.*, cytokinin and abscisic acid). Means for inhibiting or enhancing expression of genes involved in the synthesis of these regulators is also described.

Indeed, the Examiner has cited the Li *et al.* reference, discussed above, which shows that tissue specific expression of genes controlling cytokinin synthesis was known in the art at the time of the invention. In Li *et al.* , the authors showed that overproduction of cytokinins in specific tissues and organs of transgenic tobacco plants produced a number of morphological and physiological changes.

In light of the above, applicants respectfully submit that the assertion that the specification does not provide teaching with regard to promoters or genes useful in the present invention cannot be maintained. Although some experimentation may be required to identify certain promoters or genes, the Examiner fails to show that such experimentation was not entirely routine for one of skill in the art at the time of the invention. Withdrawal of the rejection for alleged lack of enablement is respectfully requested.

Rejection under 35 U.S.C. § 103(a)

The rejection of the claims for allegedly being obvious over Amasino *et al.* (US Patent No. 5,689,042) is respectfully traversed.

It is well settled that to establish a *prima facie* case of obviousness, the Examiner must meet three basic criteria. First, the Examiner must show that there is some suggestion or motivation, either in the cited references themselves or in the knowledge generally available to

one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, the Examiner must show a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991) and MPEP § 2142. To support the rejection, the examiner must "present a convincing line of reasoning as to why the artisan would have found the claimed invention to have been obvious in light of the teachings of the references." *Ex parte Clapp*, 227 USPQ 972, 973 (Bd. Pat. App. & Inter. 1985) and MPEP § 2142.

In the present rejection, the Examiner relies on Amasino *et al.*, which teaches use of the SAG12 promoter and IPT gene to inhibit leaf senescence in plants. As noted by the Examiner, the reference fails to disclose use of such constructs in maize. The Examiner then goes on to allege that one of skill would be motivated to modify the teachings of this reference because programmed cell death in the lower floret was known. As noted above, however, to establish a proper case of *prima facie* obviousness, the Examiner must show what in the prior art would lead of skill to have reasonable expectation of success. The Office Action provides no reasoning or evidence to show why one of skill would be motivated to alter the Amsino *et al.* teachings or why such a person would have a reasonable expectation of success. In the absence of such a showing, the rejection is improper and should be withdrawn

Finally, applicants note that the same claims have been rejected for lack of enablement at the same time being rejected for allegedly being obvious over the prior art. To be obvious, the prior art, even without the benefit of an applicant's disclosure, must teach one of skill how to practice the invention. To lack enablement, the application, in combination with the prior art, must fail to teach one of skill how to practice the invention. It is simply not possible for Amasino *et al.* to teach one of skill how to practice the invention, while the combination of the teachings of the same reference and the present application does not.

This logical non sequitur has been expressly disapproved by the Federal Circuit. *See In re Dow Chemical*, 5 USPQ2d 1529, 1531 (Fed Cir. 1988). As indicated by the Federal Circuit in Dow, simultaneously pursuing both arguments demonstrates substitution of a proper

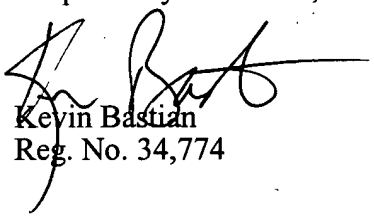
obviousness analysis with an "obvious to try" standard, which has been repeatedly rejected by the Board of Appeals and the Federal Circuit.

In light of the above, the rejection under §103(a) is clearly improper. Withdrawal of the rejection is respectfully requested.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested. If a telephone conference would expedite prosecution of this application, the Examiner is invited to telephone the undersigned at 415-576-0200.

Respectfully submitted,



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